REMARKS/ARGUMENTS

Claims 1-21 have been previously cancelled.

Claims 22-26 remain in this application.

In response to the Office Action of April 10, 2007, Applicant requests re-examination and reconsideration of this application for patent pursuant to 35 U.S.C. 132.

Rejections under 35 USC 112 First Paragraph

Claims 22-26 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of diagnosing multiple sclerosis by determining a level of anti-MBP IgG or a combination of anti-MBP IgG and anti-MBP IgM, is deemed not to reasonably provide enablement for diagnosing multiple sclerosis by determining only a level of anti-MBP IgM.

Accordingly, in order to expedite prosecution, the claims have been modified to be commensurate in scope with the disclosure, to the extent alleged by the Examiner. It is stressed however, that Applicant reserves the right to pursue the additional coverage in a continuing application.

Rejections under 35 USC 112 Second Paragraph

Claims 22-26 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 is deemed to be vague and indefinite because it recites a method for diagnosing or monitoring multiple sclerosis. It is unclear to the Examiner which is being done. Further, diagnosing would involve a definitive yes or no for having the disease, whereas monitoring would involve determining a progression and would also require samples taken at different time intervals. Therefore, it is unclear to the Examiner how both are performed.

Claim 22 the recitation "blood products" is deemed to be vague and indefinite.

Accordingly, the Examiner's suggestion to delete the term in favor of --serum or plasma--, has been adopted.

Claim 22 the recitation "about" is indicated as being a relative term which renders the claim indefinite. The term "about" is not defined by the claim, the specification does not provide a definition for the term. The specification on page 26, lines 10 - 12 discloses "the clinical objectives of high

sensitivity (77%). See other deficiencies within the claims directed to the term "about".

Claim 22, line 5 is deemed vague and indefinite because it is unclear if applicant intends that the body fluid further includes blood, blood products and saliva (i.e. a traumatic lumbar puncture wherein the cerebrospinal fluid would also include blood) or if the body fluid is one of the fluids selected from blood, blood products and saliva. The specification on page 33, line 20 discloses that the body fluid is blood or blood products. The Examiner suggests that if applicant intends that the body fluid is blood, blood products or saliva, it is recommended to amend the claim to clearly recite this and to place the body fluid in a proper Markush recitation.

Accordingly, the claim has been so amended.

Claim 22 is deemed to be vague and indefinite because it is unclear what applicant is detecting. Step (b) is questioned by the Examiner, in that the Examiner states that it appears to be an assay for binding myelin basic protein. However, it is unclear to the Examiner how an assay binds myelin basic protein. The Examiner asks whether applicant intends to perform an ELISA wherein an antibody is immobilized to capture myelin basic protein or does applicant

intend that an ELISA is performed wherein immobilized myelin basic protein captures something or does applicant intend something else? Regarding step (c), the Examiner opines that it appears to be determining a level of one autoantibody and step (d) only recites comparing autoantibody. It is therefore deemed to be unclear what relationship exists between steps (b) and (c) and how is step (b) (which appears to be determining MBP) used in step (d)?

Regarding claim 22 step (c), lines 13-14 "the recitation specific for said at least one autoantibody in said sample" is vague and indefinite. It is unclear to the Examiner what applicant is doing. How is the at least one autoantibody specific for the at least one autoantibody in the sample? Please clarify.

Claim 22 step (d) is deemed to be vague and indefinite because it is unclear what applicant is comparing the level of autoantibody to. Is applicant comparing the level to the myelin basic protein of step (b)? Is applicant comparing the level to a level obtained from a diseased patient? Is applicant comparing the level to a baseline or standard? Is applicant comparing the level to a level of a healthy patient?

Claim 24 is vague and indefinite because it is unclear how a method of monitoring is performed on a single sample. It appears that monitoring a disease would require obtaining different samples at different times and comparing the levels to each other to monitor a disease.

Accordingly, the claims have been amended to eliminate the vagueness and ambiguities highlighted by the Examiner. No new matter has been added by these amendments. See page 34 for a definition of "statistically significant" and page 35 for a discussion of the immobilized myelin basic protein.

Rejection under 35 USC 103(a)

Claims 22-24 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Voumvourakis et al (Detection of anti-MBP in the serum of patients with multiple sclerosis, Greek Microbiology Organization Newsletter (1992) 37, 666-672) in view of Pesce et al (Cationic antigens Problems associated with measurement by ELISA, Journal of Immunological methods, 87 (1986) 21-27).

Voumvourakis et al disclose a method wherein a serum sample is obtained from an MS patient. Voumvourakis et al discloses that the sample is subjected to an ELISA assay wherein an immobilized myelin basic protein (MBP) (cationic

protein) is used to capture and determine levels of anti-MBP IgG and anti-MBP IgM. Voumvourakis et al discloses that the determined levels are compared to healthy controls (p. 668) and statistically significant levels are determined for the IgG antibodies.

Voumvourakis et al differ from the instant invention in failing to teach the utilization of heparin to reduce non-specific charge interactions with MBP.

Pesce et al disclose the use of heparin to reduce non-specific charge interactions of cationic proteins that plague the sensitivities of ELISAs. Pesce et al disclose that non-specific reactivity of the cationic protein could almost completely be eliminated by carrying out the antibody-antigen incubation in the presence of heparin (p. 23) and further discloses that the use of heparin allows for the enhancement of antigen-antibody reactions because of neutralization of the positive charges on the antigen (p. 27).

The Examiner asserts that it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the use of heparin as taught by Pesce et al into the method of Voumvourakis et al because Pesce et al shows that non-specific reactivity of the cationic protein (MBP is cationic) can almost completely be eliminated by carrying out

the antibody-antigen incubation in the presence of heparin and further discloses that the use of heparin allows for the enhancement of antigen-antibody reactions because of neutralization of the positive charges on the antigen. The Examiner goes on to opine that one of ordinary skill in the art would have a reasonable expectation of success incorporating heparin as taught by Pesce et al into the method of Voumvourakis et al.

Claims 25 and 26 further stand rejected under 35 U.S.C. 103(a) as being unpatentable over Voumvourakis et al and Pesce et al in view of Landry (5,736,343) or Bishop et al., (Clinical Chemistry 2"d edition, 1992, pages 70-71).

See above for the teachings of Voumvourakis et al and Pesce et al. Voumvourakis et al and Pesce et al differ from the instant invention in failing to teach first and second samples obtained at different times.

Landry discloses that it is known in the art that for monitoring the course of a disease in a subject that first and second samples are taken at different time intervals and comparing the amounts determined in order to indicate the course of the disease (col 15).

Bishop et al discloses that it is known in the art for monitoring that a test result is compared with values previously obtained from the same patient (col 71).

The Examiner concludes that it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate comparison steps to previously obtained values because both Landry and Bishop show that it is known in the art to compare values to previous obtained values in order to provide the monitoring of a disease. Thus, one of ordinary skill in the art would have a reasonable expectation of success comparing the values to previously obtained values to monitor the progression of a disease.

It is submitted that Voumvourakis et al. merely teach a method for the detection of anti-MBP (myelin basic protein) in the serum of patients with MS, and failed to recognize the problems associated with non-specific interactions related to the use of an ELISA assay utilizing immobilized MBP for determining the presence of anti-MBP IgG, or a combination of anti-MBP IgM and anti-MBP IgM .

The Examiner asserts that it would have been obvious to one of ordinary skill in the art to incorporate the use of heparin as taught by Pesce et al. into the method of Voumvourakis et al. because Pesce et al. show that non-specific reactivity of the

cationic protein can almost be completely eliminated by carrying out the antibody-antigen incubation in the presence of heparin and further discloses that the use of heparin allows for the enhancement of antigen-antibody reactions because of neutralization of the positive charges of the antigen.

While it is possible to combine the teachings of these references, the Examiner is respectfully reminded that the fact that references can be combined or modified does not render the resultant combination obvious unless the prior art suggests the desirability of the combination (see MPEP 2143.01). Furthermore, Pesce is only directed toward non-specific interactions of cationized BSA cationized BGG.

While Pesce et al indicates that other polycationic molecules might share what he terms "unique" properties, it is respectfully submitted that a skilled artisan, absent the instant inventor's own disclosure, would not look to promulgating an obviousness rejection by utilizing the combination of Voumvourakis et al and Pesce et al, since there is no teaching or suggestion that the instant inventor's unique combination would fall within this disclosure. There is no intrinsic or inherent suggestion in the references to instigate this combination, other than the impermissible use of hindsight.

Even under the new guidelines, obvious to try is not a valid basis for an obviousness holding. The same unpredictability under the Wands factors that are the test of an enabling disclosure should reasonably be applied when determining whether a rejection is "enabled" or whether it requires an impermissible hindsight reconstruction based upon the Applicants' disclosure. Applicants respectfully submit that the situation in the instant application is analogous to the situation in the application of Geiger (*In re Geiger* (2 USPQ2d 1276)) and assert that the Examiner has only established a case for "obvious to try" rather than establishing obviousness of the claimed invention.

It is respectfully submitted that a holding of obviousness under 35 USC 103(a) is improper in this fact situation, and that the rejection ought to be withdrawn.

SUMMARY

In light of the foregoing remarks and amendment to the claims, it is respectfully submitted that the Examiner will now find the claims of the application allowable. Favorable reconsideration of the application is courteously requested.

Respectfully submitted,

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